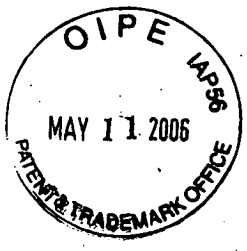

PLEASE STAMP TO ACKNOWLEDGE RECEIPT OF THE FOLLOWING:

In Re Application of: Sylvie ROUX et al.

Application No.: 10/662,808 Group Art Unit: 1632

Filed: September 16, 2003 Examiner: Unknown

For: IN VIVO MODULATION OF NEURONAL TRANSPORT

1. Petition for Extension of Time (Three Months)
2. Response to Notice to File Missing Parts of Application
3. Executed Declaration/Power of Attorney
4. Substitute Specification (Attachment A to Preliminary Amendment)
5. Marked-up Copy of Substitute Specification (Attachment B to Preliminary Amendment)
6. Submission of Replacement Drawings
7. Replacement Drawings for Figures 2 and 6A-11E
8. Transmittal Letter
9. Preliminary Amendment
10. Computer-Readable Form (CRF) Copy of Sequence Listing
11. Paper Copy of Sequence Listing (Attachment C to Preliminary Amendment)
12. Statement to Support Sequence Listing Submission
13. Copy of Notice to File Missing Parts
14. Recordation Form Cover Sheet
15. Executed Assignment
16. Check for $2,436.00 ($950 Extension Fee; $770 Filing Fee; $546 Additional Claims Fee; $130 Late Fee; $40 Assignment Recordation Fee)

Dated Monday, May 3, 2004 **Docket No.: 03495.0174-02000** (Due Date: Sunday, May 2, 2004)

Timothy B. Donaldson/Joanne C. Allen - Mail Drop 815 Reston

PATENT
Customer No. 22,852
Attorney Docket No. 03495.0174-02000

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	
Sylvie ROUX et al.	)	
	)	
Application No.: 10/662,808	)	Group Art Unit: 1632
	)	
Filed: September 16, 2003	)	Examiner: Unknown
	)	
For: IN VIVO MODULATION OF NEURONAL TRANSPORT	)	
	)	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

PRELIMINARY AMENDMENT

Please amend the above-identified patent application as follows:

Amendments to the Specification are included in this paper.

Amendments to the Claims are reflected in the listing of claims in this paper.

Remarks follow the amendment sections of this paper.

Attachments to this amendment include a Substitute Specification (Attachment A), a marked-up copy of the specification (Attachment B), and a paper copy of the Sequence Listing (Attachment C).

AMENDMENTS TO THE SPECIFICATION:

Please replace the specification, as filed, with the substitute specification filed concurrently.

Please amend the substitute specification after page 52 and before the claims by inserting the attached Sequence Listing.

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

Claims 1-31 (Canceled).

32. (Original) A method of modulating the transport in a neuron of a tetanus toxin or a fusion protein comprising a fragment C of the tetanus toxin, wherein the method comprises administering to the neuron a TrkB receptor agonist or a TrkB receptor antagonist in an amount sufficient to modulate the neuronal transport of the tetanus toxin or the fusion protein.

33. (Original) The method according to claim 32, wherein the TrkB receptor agonist is administered, thereby increasing the internalization of the tetanus toxin or fusion protein at a neuromuscular junction.

34. (Original) The method according to claim 33, wherein the TrkB receptor agonist is a neurotrophic factor that activates a TrkB receptor.

35. (Original) The method according to claim 34, wherein the neurotrophic factor is a Brain Derivated Neurotrophic Factor or a Neurotrophin 4.

36. (Original) The method according to claim 33, wherein the TrkB receptor agonist is an antibody that binds to a TrkB receptor, thereby activating the TrkB receptor.

37. (Currently amended) The method according to ~~any one of claims~~ claim 35 ~~or 36~~, wherein the internalization of the fusion protein at the neuromuscular junction is increased.

38. (Original) The method according to claim 32, wherein the TrkB receptor antagonist is administered, thereby decreasing the internalization of the tetanus toxin or fusion protein at a neuromuscular junction.

39. (Original) The method according to claim 38, wherein the TrkB receptor antagonist is an antibody that binds to a TrkB receptor agonist, thereby reducing activation of a TrkB receptor.

40. (Original) The method according to claim 39, wherein the TrkB receptor agonist is a neurotrophic factor that activates a TrkB receptor.

41. (Original) The method according to claim 40, wherein the neurotrophic factor is a Brain Derivated Neurotrophic Factor or a Neurotrophin 4.

42. (Currently amended) The method according to claim ~~42~~ 41, wherein the internalization of the tetanus toxin at the neuromuscular junction is decreased.

43. (Original) The method according to claim 40, wherein the neurotrophic factor is administered concurrently with the fusion protein.

44. (Original) A method of modulating the transport in a neuron of a tetanus toxin or a fusion protein comprising a fragment C of the tetanus toxin, wherein the method comprises administering to the neuron a GFRα/cRET receptor agonist or a GFRα/cRET receptor antagonist in an amount sufficient to modulate the neuronal transport of the tetanus toxin or the fusion protein.

45. (Original) The method according to claim 44, wherein the GFRα/cRET receptor agonist is administered, thereby increasing the internalization of the tetanus toxin or fusion protein at a neuromuscular junction.

46. (Original) The method according to claim 45, wherein the GFRα/cRET receptor agonist is a neurotrophic factor that activates a GFRα/cRET receptor.

47. (Original) The method according to claim 46, wherein the neurotrophic factor is a Glial-Derived Neurotrophic Factor.

48. (Original) The method according to claim 44, wherein the GFRα/cRET receptor agonist is an antibody that binds to a GFRα/cRET receptor, thereby activating the GFRα/cRET receptor.

49. (Currently amended) The method according to ~~any one of claims~~ claim 46 ~~or 47~~, wherein the internalization of the fusion protein at the neuromuscular junction is increased.

50. (Original) The method according to claim 44, wherein the GFRα/cRET receptor antagonist is administered, thereby decreasing the internalization of the tetanus toxin or fusion protein at a neuromuscular junction.

51. (Original) The method according to claim 50, wherein the GFRα/cRET receptor antagonist is an antibody that binds to a GFRα/cRET receptor agonist, thereby reducing activation of a GFRα/cRET receptor.

52. (Original) The method according to claim 51, wherein the GFRα/cRET receptor agonist is a neurotrophic factor that activates a GFRα/cRET receptor.

53. (Original) The method according to claim 52, wherein the neurotrophic factor is a Glial-Derived Neurotrophic Factor.

54. (Original) The method of claim 53, wherein the internalization of the tetanus toxin at the neuromuscular junction is decreased.

55. (Original) The method according to claim 47, wherein the neurotrophic factor is administered concurrently with the fusion protein.

56. (Original) A composition, comprising a TrkB receptor agonist and a fusion protein comprising a fragment C of the tetanus toxin fused to a second protein.

57. (Original) The composition according to claim 56, wherein, the TrkB receptor antagonist is a neurotrophic factor that activates a TrkB receptor.

58. (Original) The composition according to claim 57, wherein the neurotrophic factor is a Brain Derivated Neurotrophic Factor or a Neurotrophin 4.

59. (Original) A composition, comprising a GFRα/cRET receptor agonist and a fusion protein comprising a fragment C of the tetanus toxin fused to a second protein.

60. (Original) The composition according to claim 59, wherein, the GFRα/cRET receptor antagonist is a neurotrophic factor that activates a GFRα/cRET receptor.

61. (Original) The composition according to claim 60, wherein the neurotrophic factor is Glial-Derived Neurotrophic Factor.

62. (Original) A method of detecting an effect of a compound on neuronal transport, comprising administering to a neuron the compound and a fusion protein comprising a fragment C of the tetanus toxin fused to a second protein, wherein the second protein is encoded by a reporter gene, and detecting the second protein to determine the effect of the compound on neuronal transport.

63. (Currently amended) The method according to claim 62, wherein the compound is a neurotrophic factor.

64. (Original) A method of screening for a compound that reduces or prevents transport of a tetanus toxin in a neuron, comprising administering to the neuron the compound and a fusion protein comprising a fragment C of the tetanus toxin fused to a second protein, wherein the second protein is encoded by a reporter gene, detecting the second protein, and selecting the compound that reduces or prevents the neuronal transport of the fusion protein.

65. (Original) The method according to claim 64, wherein the second protein is detected at a neuromuscular junction.

66. (New) The method according to claim 36, wherein the internalization of the fusion protein at the neuromuscular junction is increased.

67. (New) The method according to claim 47, wherein the internalization of the fusion protein at the neuromuscular junction is increased.

REMARKS

Claims 32-67 are pending in this application. Claims 37 and 49 have been amended to remove multiple claim dependencies. The subject matter removed from claims 37 and 49 has been added to new claims 66 and 67. Claim 42, which inadvertently depended from itself, has been amended to change its dependency to claim 41. Claim 63 has been amended to correct a minor typographical error. Thus, this Preliminary Amendment does not introduce new matter into the specification.

Substitute Specification

The Notice to File Missing Parts of Application ("Notice") indicates that a Substitute Specification is required because page 7 does not comply with 37 C.F.R. § 1.52(a). Applicants submit with this Preliminary Amendment a substitute specification pursuant to 37 C.F.R. § 1.125(b) (Attachment A), as well as a marked up copy of the specification showing where amendments were made (Attachment B).

Specifically, the specification was amended to provide a clean copy of page 7 that complies with 37 C.F.R. § 1.52(a). In addition, pages 19-21 of the original specification were amended to add the appropriate SEQ ID NOs. On pages 7-8, the labeling of Figure 7 (i.e., "A1-A6") and Figure 8 (i.e., "A-B," "C-D," and "E-F") were updated to reflect changes made in the Replacement Drawings. Finally, on page 9, the description of Figure 2 was amended to explain that the construction of pBS:TTC is further described in Example 1. This amendment was made because in response to the Notice, Applicants have submitted a replacement drawing for Figure 2 in which the text

of Figure 2 has been deleted. Rather than add this deleted text to the description of Figure 2 in the specification, Applicants have simply referred the reader to Example 1, which contains essentially the same text that has been deleted from Figure 2. Thus, the substitute specification contains no new matter.

Sequence Listing

The Notice also indicates that the application does not comply with the requirements of 37 C.F.R. §§ 1.821-825. In response, Applicants submit a paper copy of the sequence listing (Attachment C), a computer readable form (CRF) copy of the sequence listing, and a statement that the paper copy and CRF copy are identical and that the sequence listing does not contain any new matter. By this Preliminary Amendment, Applicants also amend the specification to add the sequence listing. Thus, this application complies with 37 C.F.R. §§ 1.821-825.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: May 3, 2004

By: _____
Timothy B. Donaldson
Reg. No. 43,592